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KIDNEY HISTOPATHOLOGICAL OBSERVATIONS ON *PLASMODIUM VINCKEIVINKEI* INFECTION IN PROTEIN-MALNOURISHED MICE

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ABSTRACT

Cellular and histopathological observations were made with light microscopy during the Plasmodium vinckeivinckeiinfection in protein-malnourished mice (fed on 2% casein diet and para-aminobenzoic acid deficient diet (PABA-DD). Some glomerula swelling and an increased thickness of the basement membrane is evident with ingested malarial pigments in the capillaries of glomerula. Tubular nephrosis which is characterized by degeneration of the proximal convoluted tubules with pyknotic nuclei which were reported for the first time. Haemoglobin casts were noticed inside the tubules.

KEY WORDS: Malaria, Mice, Plasmodium Vinckei & Protein-Malnutrition

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Original Article

INTRODUCTION

Pathological changes are induced in tissues only when the invading organism has established itself. The development of lesions during infection with *Plasmodium* species is associated with 3 aspects of host-parasite relationship; (1) the magnitude of the parasitaemia, (2) the extent of the destruction of erythrocytes, and (3) the defence responses of the host against the infection, including phagocytosis and the development of immunity (John and Petri, 2006). The usual consequences of malarial infection are tropical hepatosplenomegaly and nephrotic syndrome [(1, 2)].

Protein-malnutrition eventually affects all organs and tissues of the body and their intracellar function to varying degrees[(3)]. Slowing and cessation of growth and maturation merge with advancing malnutrition into wasting and atrophy of tissues and cells [(4)].

In the case of man, it is known that both malarial infection and protein-malnutrition frequently occur together in the same community. The disease has the ability to worsen the degree protein-malnutrition [(5)].

Since almost all previous studies have been carried out using adequately nourished hosts [(6-10)], the aim of this study was to describe the gross and microscopic pathological changes produced by malarial parasite in mice maintained on low protein diet.

MATERIALS AND METHODS

Eight mice infected with *Plasmodium vinckeivinckei*and fed *ad libitum* on low protein diet (2% casein w/w) were sacrificed by exposure to diethyl ether just before death was expected to occur. Their mean parasitaemia and survival time recorded was 69.05±1.91% and 10.88±0.81 days respectively. This study did not include the mice

which survived the infection. Six uninfected mice which had been fed in the same manner on low protein diet were killed at the same time. Kidneys of all mice were removed, fixed in Helly's solution for 24 h, dehydrated, embedded in paraffin wax (56^{o}C), sectioned, stained with H and E stain and mounted with D.P.X [11] for histopathological examination by light microscopy.

RESULTS

In the uninfected mice, no evidence of pathological lesion was observed (Plate 1). The macroscopic appearance of the kidneys of the infected protein-malnourished mice were congested and dark in colour. Microscopically, there was evidence of some glomeruli swelling and an increased thickness of the basement membrane but the glomerular tuft itself looked normal (Plate 2, 4). Other glomeruli appeared to be normal. Phagocytic activity in the kidneys appeared to be low and a few cellular infiltrations had occurred. Macrophages with ingested pigments were seen in the blood vessels and occasionally in the capillaries of glomeruli (Plate 3) and intertubular connective tissues. Interestingly, tubular nephrosis characterized by proximal tubular degeneration and pyknotic nuclei was clearly evident (Plate 4, 5). Haemoglobin casts were observed inside the lumen of some tubules (Plate 4). Small amounts, seemed to be proteinous materials, have occurred in the lumen of the distal convoluted tubules. Strikingly, some malarial pigments were observed in the capsule of the kidney (Plate 6). This might have resulted from the presence of macrophages, containing ingested pigments in a capillary underneath the capsule.

DISCUSSIONS

In general, any infection can worsen the nutritional status of the host and can often lead to a precipitation of the pathogenesis and clinical signs. The swelling of the glomeruli and the increased thickness of the basement membrane have been described in other studies [7-10] and attributed to the deposition of the malarial immune complexes (antigen, antibody and complement) [12, 13]. It has been reported that the immune complex can be formed and localized in the glomeruli during human malaria [12-15] resulting in the nephrotic syndrome [1, 2]. The new and interesting observation as regards the pathological lesions in the kidneys is the evidence for degeneration of the proximal convoluted tubules (tubular nephrosis) This lesion does not appear to have been observed by previous researchers in infected mice fed on the standard diet [7-10], although a similar lesion has been detected in well-fed *Aotus*monkey infected either with *Plasmodium malariae*[16, 17] or *Plasmodium brasilianum*[17] and in human infected with *P. malariae*[18, 19]. Degeneration and necrosis of the renal tubules have been reported in patients with *Plasmodium falciparum* and this appeared to be more severe in the distal convoluted tubules than the proximal ones [20, 21]. The tubular nephrosis in infected protein-malnourished mice observed in this study is identical to the lesions of the renal tubules described in *P.malariae*infection in human and monkey. This could be attributed to the interaction of *P. vinckei*infection and the protein-malnutrition in the experimental mice. Therefore, this is another indication of the deleterious effects of the infection upon the nutritional status of the host. Even the observed malarial pigment in the capsule of the kidney does not appear to have been described by other workers, it might have resulted from the presence of pigment-laden macrophages in a capillary situated just beneath the capsule.

In conclusion, the results of this study indicate that mice infected with *Plasmodiumvinckei* offer a suitable and convenient model for histopathological studies. The deleterious effects of the infection upon the nutritional status of the host have been confirmed by histopathological investigation. Although these observations were made in a controlled experimental system, they may have some relevance to human malarial infections in protein-malnourished populations.

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APPENDICES

Plate 1: Section of Kidney from an Uninfected Protein-Malnourished Mouse No Evidence of Pathological Lesions were Observed (X 550)

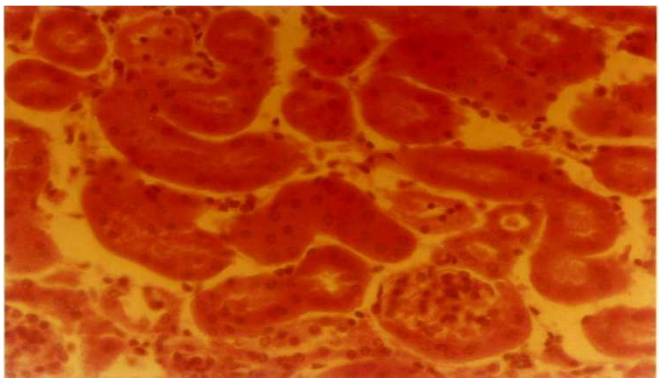

Plate 2: Section of Kidney from an Infected Protein-Malnourished Mouse Some Glomeruli Swelling and an Increased Thickness of the Basement Membrane is Evident (X 550)

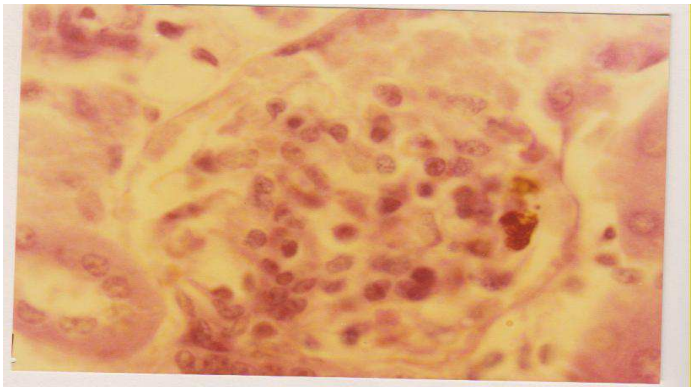

Plate 3: Section of Kidney from an Infected Protein-Malnourished Mouse Showing Ingested Malarial Pigments in the Capillaries of Glomeruli (X1375)

Plate 4: Section of Kidney from an Infected Protein-Malnourished Mouse Showing the Tubular Necrosis which is Characterized by Tubular Degeneration with Pyknotic Nuclei. Note the Haemoglobin Casts Inside the Tubules and the Increased Thickness of the Basement Membrane of the Glomeruli (X 550)

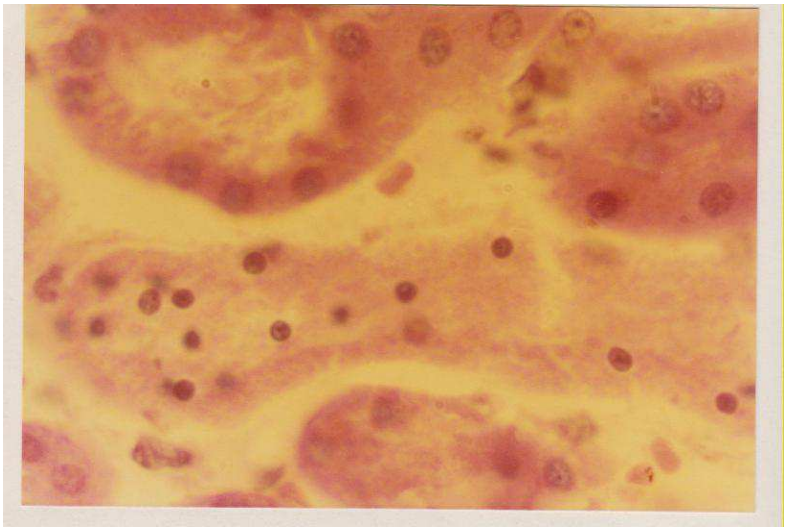

Plate 5: Section of Kidney from an Infected Protein-Malnourished Mouse Showing the Tubular Degeneration at a Higher Magnification (X 1375)

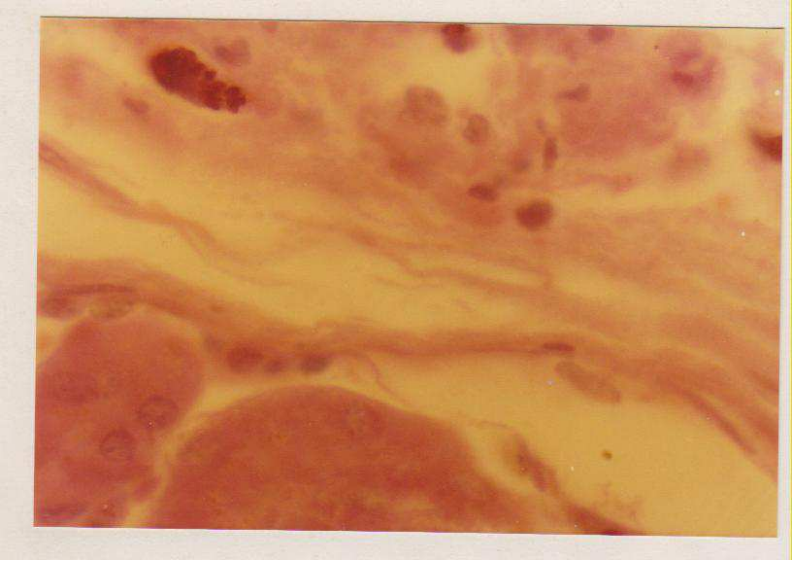

Plate 6: Section of Kidney from an Infected Protein-Malnourished Mouse Showing some Malarial Pigments in the Capsule of the Kidney (X 1375)